REMARKS

The presently claimed invention features methods for determining whether a test compound is a candidate modulator of drug resistance of a cell. Certain claimed methods entail assessing the effect of a test compound on expression of MDA-9. Other claimed methods entail determining whether a test compound binds to MDA-9 protein.

Claims 1-3 are under consideration. Claims 4-20, drawn to non-elected inventions, have been withdrawn from consideration. Claims 4 and 5 have been added. These claims are supported by the specification, for example, at pages 47-49. No new matter is added by these amendments.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 1-3 have been rejected under 35 U.S.C. § 112, first paragraph. The Examiner alleges that claims 1-3 contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicant disagrees.

Examiner's rejection is apparently based on the assumption that a protein must influence the p-gp efflux pump in order for it to modulate drug resistance. In explaining the rejection, the Examiner noted the following: (1) the MDR phenotype, exemplified by doxorubicin resistance, is often mediated by the overexpression of the p-gp efflux pump; (2) compounds have been discovered which directly interact with this pump; and (3) treatment with such compounds modulates the drug resistance of a cell over-expressing the p-gp efflux pump by binding directly to the components of the pump, not by altering its expression. The Examiner then concluded that, "[t]he instant specification provides no evidence that disabling of the p-gp pump would result in an altered level of MDA-9 expression as the level of expression of p-gp would not have been altered."

It is Applicant's position that whether disabling the p-gp pump would result in altered MDA-9 expression has no bearing on the enablement of the present claims. The Examiner has cited evidence that disabling the p-gp pump is a method known in the art to modulate drug

resistance associated specifically with the MDR phenotype. However, the Examiner has not cited any evidence that a protein **must** influence the p-gp pump in order to modulate drug resistance.

The Examiner's position, that a protein must alter the p-gp pump in order to modulate drug resistance, is at odds with the teaching in Bertram et al. (*Anti-Cancer Drugs* 9:311, 1998), previously cited by the Examiner. Bertram et al. cites a variety of roles that proteins may play in the mediation of drug resistance. For example, Bertram et al. states that calcium-binding proteins, proteins involved in alternative metabolic pathways, proteins involved in protein degradation in the proteasome, proteins involved in detoxification, hormone receptors, and tumor-associated antigens may contribute to drug resistance. Moreover, as noted previously, Bertram et al. identifies the genes in Table 2 as "mostly promising candidates for a role in the development of cellular drug resistance." Bertram et al. does not appear to suggest that any of these genes influence the p-gp pump. Thus, Bertram et al. does not support Examiner's contention that a protein **must** influence the p-gp pump in order to modulate drug resistance.

Applicant's claims are directed towards methods for determining whether a test compound is a candidate compound for modulating the drug resistance of a cell. The present invention is based, in part, on a discovered correlation between MDA-9 expression and drug resistance in three different cell lines. One skilled in the art could readily screen test compounds to identify those that alter MDA-9 expression or that bind to MDA-9, as required by the present claims. Detailed procedures for assessing the effect of a test compound on MDA-9 expression and for determining whether a test compound binds to MDA-9 are presented in the specification.

In view of the forgoing, it is Applicant's position that the present claims meet the requirements of 35 U.S.C. §112, first paragraph, and Applicant respectfully requests that the rejections under 35 U.S.C. §112, first paragraph be withdrawn.

Conclusion

Applicant asks that all claims be allowed. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

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